DEPARTMENT OF THE ARMY
U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
FORT DETRICK, MARYLAND 21701-5012

Change 1 to
USAMRDC Regulation
Number 70-25

20 April 1990

Research and Development
USE OF HUMAN SUBJECTS IN RESEARCH, DEVELOPMENT, TESTING AND EVALUATION

USAMRDC Reg 70-25, 3 May 1989, is changed as follows:

Page 7, para 3y, line 9: Change "the approving official" to "The Surgeon General."

Page 7, para 3z, line 4: Change the designation "I" to "H."

Page 14: Delete para 6a3(e); para 6a3(f) becomes 6a3(e).

FOR THE COMMANDER:

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USAMRDC Regulation
No. 70-25

3 May 1989

Research and Development

USE OF HUMAN SUBJECTS IN RESEARCH, DEVELOPMENT, TESTING AND EVALUATION

Local supplementation of this regulation is prohibited. Interim changes to this regulation are not official unless they are authenticated by the Secretary of the General Staff, USAMRDC. Users will destroy interim changes on their expiration dates unless sooner superseded or rescinded.

Paragraph Page

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*This regulation supersedes USAMRDC Regulation 70-25, 27 Apr 81, and all changes thereto.

K. CONTRACTOR USE OF HUMAN SUBJECTS, INVESTIGATIONAL DRUGS AND INVESTIGATIONAL DEVICES

L. VOLUNTEER DATA BASE

1. PURPOSE. This regulation contains policy guidance for the protection of human subjects in research conducted or supported by the U.S. Army Medical Research and Development Command (USAMRDC). It supports the Food and Drug Administration's (FDA) amendments to Title 21 of the Code of Federal Regulations (CFR) and the Department of Health and Human Services (DHHS) amendments to Title 45 CFR. In addition, the explanation of terms directly reflects upon those published in Department of Defense Directive 3216.2. Where possible, this regulation correlates with AR 40-38, Clinical Investigation Program.

2. APPLICABILITY. This regulation is applicable to USAMRDC and its subordinate units including, but not limited to, contracts and grants supporting research and related activities in which human subjects are involved. Compliance with this regulation will in no way render inapplicable pertinent federal, state, or local laws or regulations.

3. EXPLANATION OF TERMS.

a. Approving Official - A military commander or civilian director of an organizational element of a DA component who has been delegated authority to approve the use of human subjects in research.

b. Associate investigator - A person who may be involved in the execution of research, but does not have overall primary responsibility.

c. Certificate of Assurance - See Protection of Human Subjects Assurance/Certification/Declaration.

d. Consent - See Informed Consent.

e. Contractor/Grantee Research - DOD research wherein the principal investigator and all co-investigators of the study are neither active military nor full-time employees of DOD but the research does involve DOD funds.

f. Development - Systematic use of scientific knowledge, directed toward--

(1) Significant improvements in or creation of useful products to meet specific performance requirements.

(2) Development of components for incorporation in end items to meet specific performance requirements.

(3) Construction of hardware for test purposes to determine feasibility of technical approaches.

(4) Formulation and refinement of techniques and

procedures which improve Army capabilities in nonmateriel areas.

g. Epidemiologic-assessment interview - For the purpose of this regulation, this term means questioning of a serum positive member of the Armed Forces for the purposes of medical treatment or counseling, or for epidemiologic or statistical purposes. See AR 600-110.

h. Epidemiological surveys - For the purpose of this regulation, the term means studies of the distribution and determinants of disease frequency in humans, involving no more than minimal risk in which research data is not linked to personal identifiers. Epidemiological surveys focus on "ills" of a population rather than on persons.

i. Evaluation - The subjective determination of the military value of a hardware item or system, real or conceptual, to the user. There are three types of evaluation: Developer, technical, and operational. See AR 70-10 for more detail.

j. Expedited review procedures - Those procedures used in research involving no more than minimal risk and those used for minor changes in approved investigations (see Appendix H). These procedures minimize time required for review.

k. Experimental subject - See human subject.

l. Extramural research - USAMRDC-sponsored research conducted in universities, nonprofit research institutes, commercial firms, other U.S. Government activities, and foreign governments and organizations. Extramural research may be supported by contracts, grants, and intragovernmental transfer of funds.

m. Health care personnel - Military personnel, civilian employees, or contract personnel (including military and civilian staff members, assigned to, employed by, or appointed to the Uniformed Services University of the Health Sciences) who provide patient care or patient care support services in military MTFs and DTFs.

n. Health and Human Services Certificate of Assurance - See Protection of Human Subjects Assurance/Certification/ Declaration.

o. Human subject -

(1) A living individual about whom an investigator conducting research obtains data through interaction with the individual, including both physical procedures and manipulations of the subject or the subject's environment.

(2) Minor (child). A person who has not attained the legal age for consent to treatments or procedures involved in research, under the applicable laws and jurisdiction in which the research will be conducted.

(3) Human subjects may be thought of as direct objects of research when the research is to determine the effects of a

system on humans (for example, the effects of a weapon's blast on hearing) or as indirect objects when a test is conducted to determine how humans affect the ultimate performance of a system (doctrine concepts, training programs).

(4) The term "human subject" does not apply to persons participating in epidemiological studies; to the performance of normal, accepted military duties by military personnel assigned to provisional or test units executing approved test and evaluation programs; to military personnel participating in accepted and approved force, unit, crew, or individual combat readiness, effectiveness, proficiency, or fitness exercises; or to civilian or military personnel who are trained to test (e.g., test pilots and test engineers) and are assigned to duty positions that specifically call for that specialty training.

p. Human Subjects Research Review Board (HSRRB) - The principal body of the Office of The Surgeon General (OTSG) for the assessment of practices and procedures by which DA employs human subjects in research and clinical investigation activities.

q. Human Use Committee (HUC) - A body set up to provide initial and continuing review of research involving the use of human subjects. A HUC is fundamentally similar to an institutional review board (IRB) (45 CFR 46), but has somewhat different authority as compared to an IRB. Within DOD, authority to approve the use of human subjects in research is vested in commanders. Commanders act on the recommendations of validly constituted HUCs. Outside DOD, IRBs tend to be vested with this authority. Paragraphs 9 and 10 describe the membership, functions, and operations of a HUC.

r. HURRAO - refers to the Human Use Review and Regulatory Affairs Office at HQ, USAMRDC.

s. Informed consent - The legally effective agreement of the subject or the subject's legally authorized representative for the subject to participate in research covered by this regulation. Informed consent includes, when appropriate, those elements listed in paragraph 7 of this regulation.

(1) Permission. The agreement of parent(s) or guardian to the participation of their child or ward in research.

(2) Guardian. An individual who is authorized under applicable state or local law to consent on behalf of a minor (child) to general medical care.

(3) Assent. A minor's (child's) affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

t. In-house research - Research conducted in USAMRDC institutes/laboratories, or by military, civilian, or USAMRDC-supported investigators conducting research and development at a facility not under the cognizance of USAMRDC.

u. Institution - Any public or private entity or agency (including Federal, State or other agencies).

v. Investigational drug - A drug may be considered investigational when the composition is such that--

(1) Its proposed use is not recognized for the use under the conditions prescribed; or its proposed use is not recommended or suggested in its approved labeling. Experts qualified by scientific training and experience evaluate the safety and effectiveness of drugs to make this determination.

(2) Its use has become recognized as investigational, as a result of studies to determine its safety and effectiveness for use under such conditions.

w. Investigational medical device -

(1) A device that is not generally used in the diagnosis, cure, mitigation, treatment or prevention of disease in humans, and recognized as safe and effective.

(2) Research is usually, but not necessarily, initiated to determine if the device is safe or effective.

x. Legally authorized representative - A person or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's taking part in the procedures involved in the research.

y. Medical monitor - This person is a physician qualified by the training and/or experience required to provide care to research subjects for conditions that may arise during the conduct of the research, and who monitors human subjects during the conduct of research. For the purpose of this regulation, the principal investigator may function as the medical monitor only in situations in which no other physician is available. Such action will be documented by the recommending HUC and approved by the approving official. In contractor performed research, a military or DA civilian physician may be the medical monitor; however, this is usually a contractor provided resource.

z. Minimal risk - The proposed risks are not considered greater than those encountered in the subject's daily life or during routine physical or psychological examinations. Appendix I contains examples of minimal risk studies. Research involving investigational drugs is always considered more than minimal risk.

aa. Non-U.S. citizens - Foreign nationals, excluding U.S. military personnel on active duty.

bb. Personal identifier - A method or system which definitively links data to the individual from whom or about whom it pertains. The two most common personal identifiers are name and Social Security number.

cc. Principal investigator - A person, regardless of title, who is primarily responsible for the actual execution of the research.

dd. Prisoner - Any person (adult or minor) involuntarily confined or detained in a penal or correctional institution (for example, jail, workhouse, house of detention, prison, military stockade, or brig). The term is intended to encompass individuals detained pending arraignment, trial, or sentencing; and prisoners of war (including detained personnel). The term does not include individuals voluntarily confined nor those persons subject to civil commitment procedures that are not alternatives to criminal prosecution.

ee. Protection of Human Subjects Assurance/Certification/ Declaration - A document issued by the Office for Protection from Research Risks, DHHS, in which that office acknowledges that a research institution has established policies and procedures consistent with 45 CFR 46. (See Appendix G).

ff. Protocol - The written, detailed plan by which research is to be conducted. (See appendix C for an outline of what should be included in a research protocol.) The plan contains, as a minimum --

(1) The objectives of the project.

(2) The information to be collected.

(3) The means by which it will be collected and evaluated; an assessment of potential risk and benefits to subjects; safety measures, and other means to be used to reduce any risk to subjects.

gg. Research - A systematic investigation that is designed to develop or contribute to generalizable knowledge. The term does not include individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercise (DODD 3216.2)

hh. Research, development, test, and evaluation (RDTE) - Includes those categories of research and development included in Program 6, Research and Development, and operational systems development contained in the Five-Year Defense Program.

ii. Serum positive member of the Armed Forces - For the purposes of this regulation, this term means a member of the Armed Forces who has been identified as having antibodies to a virus associated with the acquired immune deficiency syndrome (AIDS).

jj. Test - A process by which data are accumulated to serve as a basis for assessing the degree to which an item or system meets, exceeds or fails to meet the technical or operational properties required. AR 70-10 has a more detailed discussion of the RDTE type tests.

kk. Test article - For the purpose of this regulation, this term means any investigational drug or investigational medical device intended for human use. In addition, food additives, color additives and electronic products intended for human use will be considered test articles.

ll. Volunteer Data Base - See Appendix L for a discussion of the composition of the Volunteer Data Base.

4. BASIC POLICIES.

a. Safeguarding the rights and welfare of human subjects participating in in-house research is primarily the responsibility of the approving official who receives, or is accountable to USAMRDC for, the funds awarded for the support of the project.

b. Safeguarding the rights and welfare of human subjects in research funded or supported by USAMRDC is primarily the responsibility of the contractor/grantee who receives, or is accountable to USAMRDC for, the funds awarded for the support of the project.

c. In order to provide for the adequate discharge of human subject protection responsibility, it is the policy of USAMRDC that research involving human subjects normally be documented by a scientific review process and presented before a Human Use Committee. Documentation of both scientific and human use review must be included in the submission of protocols to HURRAO.

d. The HUC shall determine and document whether the subjects will be placed at risk. Assessment of each protocol's risk will be documented in the appropriate HUC's minutes.

e. The experiment must be such as to contribute significantly to approved research and have reasonable prospects of yielding militarily relevant results essential to an Army research program which are not obtainable by other methods or means of study.

f. The rights and welfare of each subject in a study will be adequately protected (Appendix D - Declaration of Helsinki).

g. The responsibility for ascertaining the quality of the consent rests upon each principal investigator who initiates, directs, or conducts the research. It is a personal responsibility and may not be delegated.

h. The progress of the research projects will be reviewed and documented at timely intervals by the HUC. Comments of such reviews will be incorporated into the committee minutes. Copies of all USAMRDC HUC minutes will be forwarded to the Human Use Review and Regulatory Affairs Office (SGRD-HR).

i. No contract research involving human subjects shall be awarded to an individual unless he or she is affiliated with or sponsored by an organization which can and does assume

responsibility for the subjects involved (45 CFR 46).

j. The number of subjects used will be kept at minimum consistent with the criteria for validity and reliability in the scientific discipline(s) utilized in the research. Wherever feasible, both males and females should be utilized as subjects. Exceptions would be studies of diseases which exclusively affect only one sex or where involvement of pregnant females, or females who may become pregnant, may expose the fetus to undue risks. If either males or females are to be excluded, a clear rationale should be provided for their exclusion.

k. The research will be conducted so as to avoid all unnecessary physical and mental suffering and injury.

l. No research will be conducted if there is any reason inherent to the nature of the project to believe that death or disabling injury will occur.

m. Proper precautions will be taken and adequate facilities provided to protect the subjects against all foreseeable disability, or death that might result from study participation. This includes, but is not limited to, adequate on-site emergency apparatus, facilities, hospitalization, and medical treatment as may be required.

n. The research will be conducted only by scientifically qualified persons. The highest degree of skill and care will be required during all stages of the research (USAMRDC Reg 40-66).

o. Subjects will have no physical or mental diseases which will make the proposed research more hazardous for them than for normal healthy persons unless such condition is a necessary pre-requisite for the particular study involved. This determination will be made by the principal investigator with, if necessary, competent medical advice. In any such case, the use of human subjects with such pre-existing conditions must have been specifically described and justified in the scope of the work to be performed by the protocol or contract. Large-scale distribution studies involving the use of questionnaires and interviews are exempt from this policy. Appendix I describes exempt research categories.

p. The principal investigator will terminate the research at any stage if he or she has probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him or her, that continuation is likely to result in serious injury, disability, or death to the subject. This policy is not intended to prohibit the evaluation of treatment modalities until efficacy can be appropriately evaluated on a sound statistical basis.

q. Unless referenced otherwise in the protocol, a medical monitor will be responsible for the medical care of the subjects. The monitor will have authority to terminate the research at any time that he or she believes that death, serious injury, or disability is likely to result. The monitor is also responsible

for terminating the participation of individual subjects if a change in the subject's medical status places the subject at increased risk.

r. All research terminations and significant adverse reactions (that are clearly related to the study being performed) will be reported by the principal investigator to the approving official and HUC, and, where applicable, to the Contracting Officer's Representative (COR). The approving official, or his or her designee, will be responsible to report such actions to the Chief, Human Use Review and Regulatory Affairs Office, USAMRDC.

s. Prisoners of war or detainees will not be used as research subjects under any circumstances.

t. A subject's hospitalization costs in a military care facility will be waived if he or she normally would not be hospitalized for treatment, but is requested to enter the hospital for research or follow-up activities related to the research.

u. Studies that involve special classes of human subjects--minors, pregnant women, institutionalized mentally infirm, mentally disabled, or prisoners--must be justified in that the information sought is not obtainable from any other source.

v. It should be recognized that Title 10, Section 980 of the United States Code directs that funds appropriated to the DOD may not be used for research involving a human being as an experimental subject unless:

(1) The informed consent of the subject is obtained in advance; or

(2) In the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance.

w. When reasonable, provisions should be made for a post-participation debriefing of subjects.

x. Waiver and advance determinations. Certain exceptional circumstances might make it necessary to request an exception from the Commander, USAMRDC to one or more of the policies or procedures contained in this regulation. In such cases, full justification must be provided as to why such policies or procedures should be waived. Advance determinations may from time to time be made identifying those projects or classes of projects; biomedical methods and procedures, and/or other situations in which human subjects are involved, to which specific portions of this regulation shall not be applicable. Requests or recommendations for advance determinations should be forwarded, in writing, with full justification thereof, to Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD-HR, Fort Detrick, Frederick, MD 21701-5012.

y. Concerning the study or evaluation of investigational drugs, all users of this regulation will comply with the Code of Federal Regulations, Title 21, Part 312, AR 40-7, and AR 70-25. See also Appendixes E and F for more information.

z. Concerning the study or evaluation of investigational medical devices, all users of this regulation will comply with the Code of Federal Regulations, Title 21, Part 812, AR 40-7, and AR 70-25. See also Appendixes E and F for more information.

aa. Within USAMRDC, minimal risk studies (see definition) may be implemented based on decision of approving official of the USAMRDC Laboratory after assessment of risk and recommendation of approval by the local scientific and human use committees. One copy of all minimal risk protocols together with approved HUC minutes will be forwarded to HQ, USAMRDC, ATTN: SGRD-HR for information within fifteen working days of approval by the approving official. Studies involving more than minimal risk will be forwarded after local scientific and human use approval by the approving official to USAMRDC, ATTN: SGRD-HR for presentation to the Human Subjects Research Review Board (HSRRB).

bb. With the exception of radiopharmaceutical dosage forms, the pharmacy is the appropriate storage area for all investigational drugs and devices in medical care facilities. When appropriate, USAMRDC principal investigators should consult the pharmacy officer concerning recording, labeling, storage and dispensing criteria. In research facilities (laboratories, institutes, etc.) which do not have a pharmacy, the principal investigator will maintain or designate a specific custodian to maintain accountability for all investigational drugs and devices. AR 70-65 prescribes policy and procedures for the management of controlled substances, ethyl alcohol, and hazardous biological substances used in executing the Army's research, development, test, and evaluation program.

cc. For studies involving alcohol and drug abuse, when protection of the confidentiality of the data is critical, the principal investigator should, with the concurrence of The Surgeon General, obtain a Confidentiality Certificate issued by the Secretary, Department of Health and Human Services (DHHS). Only the Deputy Chief of Staff for Personnel (DCSPER) has approval authority for studies involving alcohol and drug abuse programs. (AR 40-38).

dd. Psychologists who conduct behavioral research (psychological, physiological, and comparative) shall, in such research, maintain respect for the dignity and worth of the individual and strive for the preservation and protection of fundamental human rights. The principles to be adhered to are those contained in the American Psychological Association's Ethical Principles of Psychologists (January 1981), with special regard for Principle No. 9.

ee. Organs, tissues or tissue fluids obtained at autopsy shall not be used for research or investigational purposes without the expressed written consent of the next of kin. It

should be noted that a general autopsy consent is not, in itself, sufficient. If autopsy tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue. (DODD 6465.2).

ff. Organs, tissues or tissue fluids obtained from a surgical procedure shall not be used for research or investigational purposes without the expressed written consent of the patient or the patient's legal representative. It should be noted that a consent to perform surgery is not, in itself, sufficient. If excised tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

gg. If an advertisement is to be used to recruit volunteers for a study, the content of that advertisement must be approved by the HUC to ensure that the information is not misleading. The advertisement should be limited to name and address of the clinical investigator, purpose of the research and summary of eligibility criteria, straightforward and truthful description of benefits, and location of research and person to contact for further information.

5. GENERAL REQUIREMENTS FOR INFORMED CONSENT. No investigator may involve a human being as a subject in research covered by this regulation unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

6. ELEMENTS OF INFORMED CONSENT.

a. Basic elements of informed consent. In seeking informed consent, the following information shall be provided to each subject. Investigators should use DA Form 5303-R (Appendix B).

(1) Title of the study and location (specify address) where it is to be conducted.

(2) Name of principal investigator, and associate(s), if applicable, conducting the study.

(3) A statement that the study involves research and an explanation of the purpose of the research. In general, the structure of the informed consent should:

(a) Be readable (short, clear, simple, declarative

sentences).

(b) When feasible, use non-medical language that is easily understood by the subject. One must take into consideration the age group, reading level and education of prospective subjects.

(c) Provide a translation of the consent form for subjects enrolled in a study who do not comprehend English.

(d) Speak to the research subject in the first person singular, "I" and/or "you."

(e) Always be explicit in detailing inclusion/exclusion criteria.

(f) Provide a copy of the consent document to the subject/legal representative. There should be a statement in the document to the effect that the subject/legal representative will be provided a copy.

(4) A statement indicating the expected duration of the subject's participation (the number of hours, days, etc.).

(5) A description of the procedures to be followed and identification of any procedures which are experimental.

(a) Briefly explain the study design relative to what will be done to the subject (in blind or double-blind studies, subjects must be informed that they may receive either the experimental modality or a placebo). If a placebo is used, its contents should be described.

(b) Specify what is required of the subject (hospital visits, blood donation, etc.). If blood is to be drawn, the amount(s) to be drawn should be expressed in lay terms.

(c) Describe procedures/pharmaceuticals/devices which are experimental. If an IND or IDE has been secured from the FDA, the subject should be advised that the IND or IDE is permission for the study to be undertaken and does not indicate FDA approval for the routine use of the drug or device in the method proposed in the protocol. If a drug or device covered under an IND or IDE is involved, it must be clearly indicated in the consent form that it is investigational for the purposes of this research.

(d) Although a subject may be familiar with procedures, never assume that he or she comprehends everything.

(6) A description of any reasonably foreseeable risks or discomforts to the subject.

(a) For studies of potential subject benefit, describe risks unique to the study; estimate their severity and likelihood; and/or compare these risks with risks which the subject might encounter in the course of his or her daily

activities. If similar research has been conducted in the past, describe the incidence of adverse effects or injuries occurring in previous subjects.

(b) For studies of no potential benefit to the subject, list all risks which are more than "minimal" (risks which are greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine medical tests).

(7) A description of any benefits to the subject or to others which may reasonably be expected from the research (mention remuneration, if any). If subjects are to be paid for participation in a research study, those payments should not be unduly large. Lump sum payments where all or most of the payment for study participation is withheld until completion of the study should be avoided since this situation may present questions of coercion of subjects to volunteer for, or continue with, a research study.

(8) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject (e.g., whether treatment is available outside of the protocol).

(9) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. It should be noted that representatives of the USAMRDC (and, where applicable, the FDA and/or U.S. Army Health Services Command) may inspect the records of the research. For studies utilizing military personnel as subjects, the following wording may be substituted: All data and medical information obtained about you as an individual will be considered privileged and held in confidence; you will not be identified in any presentation of the results. Complete confidentiality cannot be promised, particularly to subjects who are military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities.

(10) For USAMRDC sponsored research, the following statement must be incorporated into the consent form: You are authorized all necessary medical care for injury or illness which is the proximate result of your participation in this research. NOTE: Where private citizens are to be enrolled, the following statement should be included: Other than medical care that may be provided (and any other remuneration specifically stated in this informed consent), there is no other compensation available for your participation in this research study; however, you understand this is not a waiver or release of your legal rights. Contractors must provide such medical care when conducting research on civilian subjects.

(11) An explanation of (a) whom to contact for answers to pertinent questions about the research study and in the event of a research-related injury to the subject, and (b) whom to contact for answers to pertinent questions about research subjects' rights. The investigator(s) should be contacted for

(a); the HUC/IRB or legal office located closest to the research site for (b). This information should include addresses and telephone numbers.

(12) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(13) Provide space for date, signature, typed/printed name and permanent address of subject/legal representative and signature and typed/printed name of witness.

b. Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is, or may become, pregnant) which are currently unforeseeable.

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

(3) Any additional costs to the subject that may result from participation in the research.

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue to participate will be provided to the subject.

(6) The approximate number of subjects involved in the study.

(7) Precautions to be observed by the subject before and following the study.

c. The informed consent requirements in this regulation are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed for informed consent to be legally effective.

d. Nothing in this regulation is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable federal, state or local laws.

7. DOCUMENTATION OF INFORMED CONSENT. Informed consent shall be documented by the use of a written consent form, preferably DA Form 5303-R, approved by the HUC and signed by the subject or the subject's legally authorized representative and a witness. A copy shall be given to the subject/representative signing the form. If a consent form other than DA Form 5303-R is used, it shall contain the appropriate data required by the Privacy Act of 1974 (5 U.S.C. 522a; AR 340-21). This Privacy Act Statement (Appendix A) shall be signed by the volunteer/legally authorized representative and attached to the consent form.

8. HUC MEMBERSHIP.

a. Each HUC shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The HUC shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members' backgrounds, including consideration of the racial and cultural backgrounds of members and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the HUC shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The HUC shall therefore include persons knowledgeable in these areas. If a HUC regularly reviews research that involves a vulnerable category of subjects, including but not limited to subjects covered by other parts of this paragraph, the HUC should include one or more individuals who are primarily concerned with the welfare of these subjects.

b. No HUC may consist entirely of members of one profession. All HUC's within USAMRDC shall be composed entirely of employees of the Federal Government.

c. Each HUC shall include at least one member whose primary concerns are in nonscientific areas; for example: lawyers, ethicists, members of the clergy.

d. Each HUC shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

e. No HUC may have a member participate in the HUC's initial or continuing review of any project in which the member has a conflicting interest, except to provide information required by the HUC.

f. A HUC may, at its discretion, invite individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the HUC. These individuals may not vote with the HUC.

9. HUC FUNCTIONS AND OPERATIONS. With the exception of contractor research, it is the approving official's responsibility to assure that all research protocols are being conducted in an approved manner and to have a functional HUC. In order to fulfill the requirements of these regulations, each HUC--

a. Will observe written procedures for the following:

(1) Conducting the initial and continuing review of the research. Included would be reporting findings and actions to the investigator and the approving official.

(2) Determining those projects that must be

(a) Reviewed more often than yearly.

(b) Verified from sources other than the investigators that no material changes have occurred since the previous HUC review.

(3) Requiring prompt reporting to the HUC of proposed changes in the research. Each HUC will ensure that changes in approved projects (during the period for which approval has already been given) are not initiated without HUC review except to eliminate immediate hazards to the subject.

(4) Requiring prompt reporting to the HUC and approving official of unexpected problems involving risks to the subjects or others.

b. Will review proposed protocols at meetings attended by a majority of members except when an expedited review is used (see Appendix H). For the protocol to be approved, it will receive the approval of a majority of those members present.

c. Will report to the approving official any serious or continuing noncompliance by investigators with HUC requirements and determinations.

d. Will conduct continuing review of research studies at intervals proper to the degree of risk, but not less than once per year.

e. Will have the authority to observe or have a third party observe the consent process and the investigation.

f. Will maintain a current list of HUC members. Members will be identified by name, earned degrees, representative capacity and experience, such as board certifications and licenses. The information will be complete enough to describe each member's chief expected contributions to HUC reviews. Any employment or other relationship between members and the institution will be noted. A copy of that list will be provided to the Human Use Review and Regulatory Affairs Office, HQ, USAMRDC.

g. May recommend safeguards or special conditions to a protocol. If the HUC does so, the approving official may:

(1) Not reduce the safeguards or conditions if he or she approves the protocol.

(2) Require additional safeguards.

(3) Disapprove the protocol.

(4) Refer the protocol to a higher echelon approving authority and review committee.

10. CRITERIA FOR HUC APPROVAL OF RESEARCH INVESTIGATIONS.

a. In evaluating risks and benefits for research investigations, the HUC should consider only those that may result from the investigation.

b. To approve investigations covered by this regulation, the HUC will determine that all of the requirements below are met.

(1) Risks to subjects are minimized by using procedures that are--

(a) Consistent with sound investigation design and do not unnecessarily expose subjects to risk.

(b) Already being used on the subjects for diagnosis or treatment, when appropriate.

(2) Risks to subjects are reasonable in relation to anticipated benefits to subjects.

(3) In making an assessment for the selection of subjects, the HUC should take into account--

(a) The purpose of the investigation.

(b) The setting in which the research investigation will be conducted.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

(5) Informed consent will be properly documented.

(6) The plan makes adequate provision for monitoring the data collected to ensure the safety of subjects when appropriate.

(7) Adequate provisions exist to protect the privacy of subjects and to maintain the confidentiality of data when appropriate.

c. Some or all of the subjects may be vulnerable to coercion or undue influence, such as persons with acute or severe physical or mental illness, or those who are economically or educationally disadvantaged. If so, proper additional safeguards will be included in the study to protect the rights and welfare of these subjects.

11. SUSPENSION OR TERMINATION OF APPROVED RESEARCH INVESTIGATIONS.

a. A HUC will have the authority to suspend or end an approved investigation that--

(1) Is not being conducted according to the HUC's requirements. This is accomplished by continuing review of

protocols and reports by investigators.

(2) Has been associated with unexpected serious harm to subjects. This is accomplished by continuing review of protocols and reports by investigators.

b. Suspensions or terminations of research will include a statement of the reasons for the HUC's action. They will be reported promptly to the principal investigator and approving official.

12. HUC RECORDS.

a. A HUC will prepare and maintain adequate documents on HUC activities, including--

(1) Copies of all protocols reviewed, scientific evaluations that accompany the proposals, approved sample consent documents, progress reports submitted by investigators and reports of injuries and adverse reactions.

(2) Minutes of HUC meetings showing attendance; actions taken by the HUC; the vote on these actions, including the number of members voting for, against, and abstaining a decision; the basis for requiring changes or disapproving the investigation; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the HUC and the investigators.

(5) A current list of HUC members.

(6) Written procedures for the HUC.

(7) Statements of significant new findings.

b. The records required by this regulation will be retained permanently (see AR 25-400-2). Such records will be reasonably accessible for inspection and copying by authorized DA personnel and, if applicable, representatives of the FDA.

13. CONFLICT OF INTEREST.

a. It is essential that the members of the HUC continue to be perceived and, in fact, are free from conflict of interest in their daily duties, especially in regards to the protocols they review.

b. The issue of conflict of interest has been addressed by public law, DOD directive and Army regulation. The situations discussed below are merely examples of the types of activities and relationships which may result in conflict or the appearance of conflict of interest. These are by no means the only ways that conflicts arise.

(1) The potential for personal or financial gain. A committee member who is deliberating a protocol which is to be performed by a contractor, in which the member or a member of his or her immediate family is a corporate officer, stockholder, consultant or employee, could be accused of conflict of interest if he or she voted on the protocol, regardless of his or her vote.

(2) The potential for personal reward. A committee member who is affiliated with a protocol in the capacity of principal, associate or co-investigator, could be accused of conflict of interest if he or she voted on the protocol, regardless of his or her vote.

(3) Command influence. The mission (for example, the purpose of the research) should not override or obscure its methods. It is imperative that the committee, through its members, continue to be recognized as a reasonable, deliberative body, whose bias is the safety and welfare of the research subject. It is incumbent upon each committee member to assure that his or her concerns regarding the moral, ethical and legal issues of each protocol are answered to his or her satisfaction before voting according to his or her conscience.

c. Commanders and organizational heads will establish a method to ensure that each committee member is familiar with the pertinent laws and regulatory guidance regarding conflict of interest.

14. CONTRACTOR/GRANTEE RESEARCH. Any institution applying for a contract involving human subjects must provide a written assurance that it will abide by the policy for the protection of human subjects as contained in Title 45, Part 46 of the Code of Federal Regulations, as amended. If the institution currently has on file with the Department of Health and Human Services (DHHS) an approved assurance, as provided for in 45 CFR 46, a copy of this assurance (HHS Form 596, Appendix G) may be submitted and shall apply equally to the study to be performed under contract with USAMRDC. If the organization does not currently have an approved DHHS assurance, then an assurance concerning the protection of human subjects must be negotiated by the USAMRDC Contracting Officer in conjunction with the Human Use Review and Regulatory Affairs Office. The following appendixes are also included:

a. Appendix F - Guideline for Review and Approval of Contract/Grant Proposals Involving Human Subjects.

b. Appendix G - HHS Form 596 - Protection of Human Subjects Assurance/Certification/Declaration.

c. Appendix K - Contractor Use of Human Subjects, Investigational Drugs and Investigational Devices.

15. USE OF MINORS AS HUMAN SUBJECTS. An individual shall be considered to be a minor if he or she has not yet attained the age of majority specified by the laws of the state or country in which the research is being conducted. Children may be used as human subjects of research only under the conditions explained below.

a. It is not appropriate to permit a minor to participate as a human subject unless the research is concerned with:

(1) The diagnosis, treatment, prevention, or etiology of conditions not usually encountered in adults, or

(2) Any other condition from which the minor is suffering, provided there is a direct potential benefit to the child and adequate prior testing has been accomplished, or

(3) Information which cannot be obtained from any other class of subject.

b. A minor may not participate as a human subject unless the minor's parent, guardian, or other legally authorized representative has given effective third party consent.

c. In addition to securing the required third party consent, the minor, depending upon maturity, should also be consulted. Clearly, young children have neither the comprehension nor judgment to enable them to make a meaningful determination. Older children might well be able to comprehend sufficiently to understand what it is that they will be subjected to and, depending upon the circumstances, should in many cases be given the right to refuse to participate. As a child approaches the age of majority, ability to comprehend will likely become closer and closer to that of an adult and it would be improper to permit the child to participate unless he or she had also given subject assent. All of the above considerations apply to maturity of judgment and comprehension, and not solely to chronological age. Therefore, no hard and fast rules can be laid down, and careful consideration must be given to provisions which will ensure compliance with these principles. Whenever the minor's assent is obtained, it should be documented. Appendix B contains an assent form.

16. USE OF MENTALLY DISABLED OR INSTITUTIONALIZED MENTALLY INFIRM PERSONS AS HUMAN SUBJECTS.

a. It is not appropriate to permit a mentally disabled or institutionalized mentally infirm person to participate as a

human subject unless the nature of the research involved is such that it would be impossible or meaningless if mentally infirm persons were restricted from participation, or other considerations are involved. Mere convenience will never suffice as justification for the use of any such person as a human subject.

b. A mentally disabled or institutionalized mentally infirm person may not participate as a human subject unless:

(1) Legally effective subject consent has been obtained, or where the subject is legally incompetent, the subject's legally authorized representative has given effective third party consent and the subject's participation is intended to benefit the subject.

(2) The proposed research is concerned with:

(a) The diagnosis, treatment, prevention, or etiology of the particular impairment with which the subject is afflicted, or

(b) Any other condition from which the subject is suffering, providing there is a direct potential benefit to the subject and adequate prior testing has been accomplished to give assurance of acceptable risk, or

(c) The effect of institutional life upon the institutionalized mentally infirm subject, and involves no appreciable risk to the subject, or

(d) Information which cannot be obtained from any other class of subject.

c. Whenever the mentally disabled or institutionalized mentally infirm person appears to have sufficient mental capacity to comprehend what is proposed and to express an opinion as to his or her willingness to participate, his or her subject assent, even though not legally effective, must be obtained. The Commander, USAMRDC, will assure that all ethical, social, legal, and technical requirements of this regulation are met and documented prior to the approval of any protocol involving the use of an institutionalized mentally infirm person as a human subject.

17. STUDIES TO BE CONDUCTED OUTSIDE THE UNITED STATES. If a study is to be conducted outside the United States, its territories or possessions, and involves the use of other than U.S. military personnel as subjects, in addition to compliance with the provisions of this regulation, all laws, customs and practices of the country in which the study is to be conducted shall be complied with. The minimum standards to be adhered to are contained in Appendix D (The Declaration of Helsinki). The research proposal submitted for approval will document this action. In exceptional circumstances where laws, customs or practices of the country involved take exception to particular procedural provisions of this regulation (as, for example, the documentation of informed consent or the procedures by which it

is obtained), the HUC will pay special attention to these circumstances as an integral part of the proposal review and approval process. Appendix F contains guidelines for the review and approval of grant proposals involving human subjects.

18. TYPE PROTOCOLS. A "type protocol" is an in-house study plan involving the use of human subjects in a group of closely related and similar studies which differ from each other in ways which are unlikely to change the degree of risk involved. A "type protocol" does not contain a detailed plan of every possible study which might be undertaken, but includes a description of conditions under which the studies will be conducted, and the standards which will be followed to safeguard the subject. The equipment to be used, including safety equipment, must be discussed in detail, along with all conditions to which the subject will be exposed, and the deviations from normal vital signs that will be allowed prior to suspension of the subject's participation. The use of a "type protocol" is acceptable only if the conditions under which the study is being conducted are so well understood that the described safety limits are clearly acceptable for the subjects proposed to be included. All "type protocols" must be approved by The Surgeon General, through the Human Subjects Research Review Board. Approval of a "type protocol" shall be for a stated time period (generally one year), subject to renewal. "Type protocols" involving investigational drugs or devices will not be approved. Since a "type protocol" does not permit evaluation of all of the factors required prior to approval of a particular study, each individual study to be conducted under an approved "type protocol" must be evaluated individually by a documented scientific review process and supported by a HUC. A copy of the approved protocol together with a copy of documented scientific review and HUC minutes for the proposed study shall be forwarded to HQ, USAMRDC, ATTN: SGRD-HR, Fort Detrick, Frederick, MD 21701-5012. Para 4aa of this regulation describes the procedures to follow for submission of minimal and greater than minimal risk protocols.

19. CIVILIAN EMPLOYEES. When civilian employees of the Department of the Army volunteer to participate in in-house studies as human subjects, the following provisions will apply:

a. Any duty as a volunteer human subject performed during the employee's regular scheduled tour of duty will be considered as constructive duty for which straight time rates are payable. Time spent in participation outside the employee's regularly scheduled tour, or while in a leave status, will be considered as voluntary overtime for which no payment may be made nor compensatory time granted. The employee shall be so informed prior to acceptance of his or her service as a volunteer human subject, and the foregoing understanding shall be incorporated into the consent form.

b. Claims submitted to the Office of Workers' Compensation Programs, Employment Standards Administration, U.S. Department of Labor, because of disability or death resulting from an employee's voluntary participation in any study will include a citation to Title 10, United States Code, Section 4503, as the

Department of the Army authorization for use of such voluntary services.

c. All questions concerning hours of duty, pay, leave, compensation, claims, or application of other civilian personnel regulations to an employee's voluntary services, will be forwarded through appropriate channels to the Deputy Chief of Staff for Personnel, ATTN: Director of Civilian Personnel.

d. Such employees are entitled to medical care in Army medical treatment facilities in accordance with the provisions of AR 40-3, para 4-31 or 4-62.

20. IRREGULAR OR FEE-BASIS EMPLOYEES. Intermittent services of such employees are authorized. Whether such employees can be used as human subjects in any study will depend upon the statutory authority of their employment and the provisions of their employment agreement in each case. The Federal Employees Compensation Act (5 U.S.C. 751 et seq.) may well apply with respect to any injury or disease resulting from the employment, although a final determination in each case will have to be made by the Office of Workers' Compensation Programs, Employment Standards Administration, U.S. Department of Labor. Subject to such restrictions and limitations as may appear in the statutory authority under which employed, the Government may legally bear the expense of insurance premiums on the health or life of such employee whose rate of compensation is not fixed by law or regulations. In such cases, it is preferable that the Government provide an additional allowance to the employee so that the employee may purchase his or her own coverage rather than to undertake direct negotiations with insurance carriers. Such employees are entitled to medical care in Army treatment facilities in accordance with the provisions of AR 40-3, para 4-62.

21. MILITARY PERSONNEL. Military personnel may participate as human subjects. Additional compensation for such services is prohibited, except as specifically authorized by law (e.g., furnishing blood (24 U.S.C. 30), duty inside a high- or low-pressure chamber (37 U.S.C. 301a(9)), duty as a human test subject in thermal stress studies (37 U.S.C. 301a(11)).

22. OTHER PERSONS ENTITLED TO MEDICAL CARE. Retired military personnel, dependents, and others routinely entitled to medical care in military medical facilities, may participate as human subjects. Such persons may be compensated for these services as authorized by applicable directives (see 45 Comp. Gen. 649), except that retired officers of a regular component are subject to the 30-day limitation of 5 U.S.C. 5532(c)(2).

23. PRIVATE CITIZENS. It is the policy of the United States Government not to accept voluntary services, ostensibly without compensation, when such services may provide a basis for a future claim against the Government for the value of the services provided. Accordingly, any such services should be accompanied by a statement to the effect that the individual will not receive or become entitled to any compensation for these services. Such

individuals may, however, enter into an independent contractor relationship and participate for compensation as authorized by applicable directives (see 45 Comp. Gen. 649). Such individuals are entitled to medical care in Army medical treatment facilities in accordance with the provisions of AR 40-3, para 4-62. This paragraph excludes private citizens who are burn patients at the U.S. Army Institute of Surgical Research.

24. REFERENCES.

a. AR 25-400-2, The Modern Army Recordkeeping System.

b. AR 40-3, Medical, Dental and Veterinary Care.

c. AR 40-7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances.

d. AR 40-37, Licensing and Control of Radioactive Materials for Medical Purposes.

e. AR 40-38, Clinical Investigation Program.

f. AR 70-10, Test and Evaluation During Development and Acquisition of Materiel.

g. AR 70-25, Use of Volunteers as Subjects of Research.

h. AR 70-65, Management of Controlled Substances, Ethyl Alcohol, and Hazardous Biological Substances in Army Research, Development, Test, and Evaluation Facilities.

i. AR 340-21, The Army Privacy Program.

j. AR 600-110, Identification, Surveillance, and Administration of Personnel Infected with Human Immunodeficiency Virus (HIV).

k. Title 21, Code of Federal Regulations (Food and Drug Administration).

l. Title 45, Code of Federal Regulations (Department of Health and Human Services).

m. Memorandum of Understanding Between the Food and Drug Administration and the Department of Defense, Investigational Use of Drugs by Department of Defense, May 21, 1987.

n. Department of Defense Directive 3216.2, Protection of Human Subjects in DOD-Supported Research.

o. Department of Defense Directive 6465.2, Organ Disposal After Autopsy.

p. Title 10, United States Code, Section 980, Limitation on the Use of Humans as Experimental Subjects.

q. OTSG Reg 15-2, Human Subjects Research Review Board.

r. USAMRDC Reg 40-66, Quality Assurance.

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APPENDIX A

PRIVACY ACT STATEMENT
TO ACCOMPANY VOLUNTEER CONSENT FORM FOR GOVERNMENT PERSONNEL

1. AUTHORITY.

a. Title 10, United States Code, Section 3012.

b. Title 44, United States Code, Section 3101.

c. Title 10, United States Code, Section 1071-1087.

d. Executive Order 9397.

2. PRINCIPAL PURPOSE. The purpose for requesting personal information is to provide--

a. Various types of data needed to satisfy the scientific objectives of the study.

b. Minimum information necessary should you require medical treatment at any future time for a condition proximately resulting from your part in this research study.

c. Minimum information so that steps can be taken to contact you later should it be in your best interests.

3. ROUTINE USES.

a. This information may be used to--

(1) Implement health and communicable disease control programs.

(2) Provide full documentation of research studies.

(3) Conduct further research.

(4) Teach.

(5) Compile statistical data.

(6) Adjudicate claims and determine benefits.

NOTE: USE OF THIS STATEMENT IS NOT NECESSARY WHEN THE CONSENT IS DOCUMENTED ON DA FORM 5303-R

(7) Report medical conditions required by law to other Federal, state and local agencies. There is a possibility that an authorized representative from the Food and Drug Administration and the U.S. Army Medical Research and Development Command may periodically inspect these records.

b. This information may be used for other lawful purposes,

including law enforcement and litigation.

c. Even though permitted by law, when possible, this personal data will not be released without your consent.

4. MANDATORY OR VOLUNTARY DISCLOSURE AND EFFECT ON PERSON NOT PROVIDING INFORMATION.

a. Disclosure of requested information is voluntary. If the information is not furnished, or is not available from other sources, voluntary participation in this study may be prevented.

b. I understand that--

(1) A copy of the Volunteer Consent Document, together with a copy of this form, may be placed in my health records as evidence of this notice.

(2) Additional copies may be retained permanently by the investigator and by the U.S. Government.

c. I have received, or have declined to accept, a copy of the Volunteer Consent Document and a copy of this form, which I may keep.

_____

Signature

APPENDIX B

(SEE DA FORM 5303-R)

APPENDIX C

GUIDELINE FOR AN APPLICATION FOR AN IN-HOUSE RESEARCH PROJECT

1. PROJECT TITLE. Enter complete project title. If amendment, the words "Amendment to . . ." must precede project title.

2. PHASE I, II, III or IV DESIGNATED PROTOCOL. If applicable, indicate specific phase.

3. PRINCIPAL INVESTIGATOR.

4. LOCATION OF STUDY. If USAMRDC study, list all centers, clinics or laboratories where study is to be conducted.

5. TIME REQUIRED TO COMPLETE. Give month and year of expected start and anticipated completion date.

6. INTRODUCTION.

a. Medical application. Explain briefly the medical importance and possible usefulness of the project.

b. Objective(s). Brief but specific statement of project objective(s) to include, where applicable, type of study (double-blind, crossover, etc.), medications or devices to be used and type of subject population to be observed.

c. Status. What has been accomplished or published in the proposed area of study? In what way will the project relate to or differ from that which has been accomplished?

d. Study design. Multicenter, multiclinic, etc.; double-blind, cross-over, etc.

e. Bibliography. All references mentioned in the preparation of the protocol should be listed and referred to.

7. PLAN. Outline exactly what is proposed to be accomplished in enough detail to show a clear course of action. Technological validity of procedures and chronological steps should be taken. Minimum guidance for the plan includes--

a. Selection of subjects.

(1) Number of subjects. The total number of subjects expected to complete the study.

(2) Age range.

(3) Sex.

(4) Inclusion criteria. Specific and detailed guides should be presented.

(5) Diagnostic criteria for entry.

(6) Evaluations prior to entry. X-ray, physical examination, medical history, hematology, chemistry, urinalysis.

(7) Exclusion criteria. A complete list detailing which subjects are ineligible for admission into the study.

(8) Source of subjects.

(9) Subject identification. Describe code system to be used.

(10) Subject assignment. Describe by what method subjects will be assigned study medications or devices.

(11) Risks to the subject.

(12) Precautions to be taken to minimize or eliminate risks.

(13) Will any specific medical or nursing care be needed for subjects admitted to the project?

8. PROJECT MEDICATION(S) OR DEVICE(S). Describe, where applicable.

a. Complete name of all medication(s) or devices to be used, to include placebo. If medication is formulated within USAMRDC, list all components. Composition of placebo, if any.

b. Source of all medications or devices, to include placebo.

c. Place where study medications or devices are to be stored during study.

d. Dose range.

e. Dose schedule.

f. Administration.

g. Washout period. The washout or pre-drug period must be carefully noted.

h. Duration of drug or device treatment.

i. Accompanying medications. Those allowed or disqualified.

j. If needed, what antidotes must be available.

k. Labeling of study medications or devices. Include copy of label format.

9. EVALUATIONS MADE DURING AND FOLLOWING PROJECT. Evaluation may also be represented by utilizing a project schematic.

NOTE: It is very important to state in the protocol who is actually going to perform the following evaluations--

a. Specimens to be collected.

(1) Schedule and amounts.

(2) Evaluations to be made on specimens.

(3) Storage. Where, and whether special conditions are required.

(4) Labeling and disposition.

b. Clinical assessments. To include also how adverse effects are to be recorded.

c. Vital signs. When desired, and frequency.

d. Follow-up procedures.

e. Disposition of data. Where stored and for how long.

f. Who will perform the biostatistical reviews.

10. DEPARTURE FROM PROTOCOL FOR INDIVIDUAL PATIENTS.

a. When allowed.

b. Who will be notified.

11. MODIFICATION OF PROTOCOL. Describe the procedure to be followed if the protocol is to be modified.

12. EXAMPLE OF ALL REPORT FORMS FOR DATA GENERATED.

13. STATEMENT PERTAINING TO THE DISPOSITION OF UNUSED PROJECT MEDICATIONS OR DEVICES.

14. USE OF INFORMATION AND PUBLICATIONS ARISING FROM THE STUDY.

15. PERSONNEL TO CONDUCT PROJECT. List names, positions and telephone numbers of persons to be directly involved in project work. Attach a short biographical sketch. Include a resume of education, research training, and a list of publications for each person named.

16. SPECIAL OR UNUSUAL FUNDING IMPLICATIONS.

17. SIGNATURE OF PRINCIPAL INVESTIGATOR, DATE, WITH THE ACCOMPANYING STATEMENT--

"I have read the foregoing protocol and agree to conduct the study as outlined herein."

18. SIGNATURE OF APPROPRIATE APPROVING OFFICIAL AND DATE.

APPENDIX D

THE DECLARATION OF HELSINKI

1. BASIC PRINCIPLES.

a. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

b. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.

c. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

d. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

e. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

f. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

g. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.

h. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles

laid down in this Declaration should not be accepted for publication.

i. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely given informed consent, preferably in writing.

j. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.

k. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.

l. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

2. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE (CLINICAL RESEARCH).

a. In the treatment of the sick person, the doctor must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health or alleviating suffering.

b. The potential benefits, hazards and discomforts of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.

c. In any medical study, every patient -- including those of a control group, if any -- should be assured of the best proven diagnostic and therapeutic methods.

d. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.

e. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee.

f. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

3. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (NON-CLINICAL BIOMEDICAL RESEARCH).

a. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.

b. The subjects should be volunteers -- either healthy persons or patients for whom the experimental design is not related to the patient's illness.

c. The investigator or the investigating team should discontinue the research if in his or her or their judgment it may, if continued, be harmful to the individual.

d. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

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APPENDIX E

(DIAGRAM - SEE GUIDELINE FOR REVIEW & APPROVAL OF IN-HOUSE PROTOCOLS INVOLVING HUMAN SUBJECTS)

APPENDIX F

(DIAGRAM - SEE GUIDELINE FOR REVIEW & APPROVAL OF CONTRACT/GRANT PROPOSALS)

APPENDIX F

GUIDELINE FOR REVIEW AND APPROVAL OF CONTRACT AND GRANT PROPOSALS

1. KEY TERMS.

AMLO	Acquisition Management Liaison Office
AMO	Acquisition Management Office
AURO	Animal Use Review Office
CFR	Code of Federal Regulations
COR	Contracting Officer's Representative
DHHS	Department of Health and Human Services
DOD	Department of Defense
HSRRB	Human Subjects Research Review Board
HURRAO	Human Use Review and Regulatory Affairs Office
IRB	Institutional Review Board
PI	Principal Investigator
RAD	Research Area Director (4 Research Areas)
TSG	The Surgeon General
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command

2. PREPARATION OF PROPOSALS. The USAMRDC Broad Agency Announcement and specific Requests for Proposal provide prospective offerors information on the preparation of preproposals and proposals, methods by which proposals are evaluated, standards for contract administration, and regulatory guidelines for the use of animals and humans in research. The flow of preproposal submissions is: initial submission from the contracting organization to the AMO where it is given a log number, and the determination of RAD assignment is made; AMO submits preproposals to the RAD (which either accepts or declines submissions) for the determination of military relevance, program applicability, and the laboratory/institute to which preproposals are to be assigned, and; preproposals are forwarded from the RAD to the AMO which prepares paperwork for submission to the AMLO.

a. The PI will be encouraged, by the AMLO, to prepare a formal proposal in the event the preproposal meets the scientific goals of the laboratory/institute. Upon submission of the proposal, it will be reviewed by the AMLO for scientific merit. Preproposals and proposals may either be accepted or declined during the AMLO review process. Proposals that are accepted will accompany the Form 9 (Recommendation for Support of Research and Development Project) for submission by the AMLO to the AMO.

b. Up to this point, the AMO manages the processing of the Form 9 to ensure that approvals and necessary signatures are received from: the responsible RAD which either accepts or

declines a proposal, and precommits funds after proposal acceptance; the AURO and/or HURRAO, and; the comptroller for commitment of the fund site. The proposal and completed Form 9 are sent to USAMRAA for action, or remains in the AMO when proposals are to be funded as intragovernmental transfers.

c. The IRB of the contract/grant organization reviews the proposal and consent form in accordance with Title 45 CFR 46 entitled "Protection of Human Subjects," and assigns a level of risk to the study. If available at the time of submission, the PI submits evidence of local IRB approval with the proposal in the format of an HHS Form 596 (Appendix G) entitled "Protection of Human Subjects Assurance/Certification/Declaration," and the minutes of the meeting in which the review process and approval occurred. The submission of this information assures compliance with USAMRDC policy.

d. In the event the reviewing IRB does not have a multiple project assurance on file with the DHHS, as indicated in block 4 of HHS Form 596, a special assurance, as provided for in 45 CFR 46, is required to be negotiated by the USAMRAA in conjunction with the HURRAO. The determination as to whether a special assurance is required is based upon the level of risk assigned to the study by the IRB, and whether the research falls in one or more of the exempt research categories described in Appendix I of this regulation.

e. Information required of grant or contract organizations which propose the use of non-U.S. citizens in a foreign country includes: submission of a full proposal, an informed consent form, certification of ministry/minister of health approval, and documentation of review and approval of the proposal by an ethical review committee within the host country. Proposals which present minimal risk to volunteers, as determined by the local IRB, must be forwarded to HURRAO, but in most cases will not require HSRRB review. Proposals which present greater than minimal risk, as determined by the local IRB, will be presented to the HSRRB for review.

f. Proposals which involve the use of humans in research are submitted to the HURRAO from the AMO for review. The HURRAO reviews the proposal and consent form to ensure conformance with DOD directives, Army regulations, and DHHS regulations, and to ensure that validation of the human use review process by the contract or grant organization has occurred.

g. The HURRAO review process includes the writing of an administrative review. The review outlines the objective(s) of the proposal, summarizes the research design, and critiques the

proposal within the comment section. The comment section may address the need for additional information required of the PI, and deficiencies found in the proposal and consent form.

h. Should there exist outstanding human use issues in the proposal and/or consent form, e.g., lack of evidence of IRB approval, or the negotiation of a special assurance is required, the HURRAO will address these issues in letters to the PI and telephone communications. The HURRAO will furnish copies of all correspondence forwarded to the PI to USAMRAA, (or AMO for intragovernmental transfers) COR, RAD, and AMLO.

i. The HURRAO shall cite its comments, taken directly from the comment section of the administrative review, on a continuation sheet attached to the Form 9. It also lists the applicable human use provision(s) to be entered in the contract, e.g., the "Prohibition of Use of Human Subjects" provision will be entered in contracts when outstanding human use issues exist. The use of the prohibition provision permits the timely award of the contract even though all issues relative to the use of humans have not been resolved.

j. After the PI has resolved issues to the satisfaction of the HURRAO, the PI will be notified by the HURRAO, in writing, of the approval for the PI to enroll volunteers in the study. Included in the approval notification will be a statement which reads:

> "The approval of the use of humans as research subjects should not be construed as approval for funding or award of the contract. Only the Contracting Officer can award a contract and commit the federal government to the expenditure of funds."

Parallel to the PI being sent the approval notification, a DF is sent to USAMRAA requesting the contract be modified to delete the prohibition provision and to enter the appropriate human use provision.

k. Proposals which have been determined by the local IRB to be minimal risk studies or fall in one or more of the exempt research categories, as described in Appendix I of this regulation, must be forwarded to HURRAO, but in most cases will not require HSRRB review. Proposals which present greater than minimal risk to volunteers, as determined by the local IRB, require review by the HSRRB. The HURRAO will perform its review as described in paragraph 4 prior to proposal submission to the HSRRB. A proposal packet consisting of the proposal, the administrative review, and other pertinent information will be

provided to Board members at least one week prior to the scheduled meeting date. Board members will review proposals to determine that ethical, moral and legal standards are appropriate for the practices and procedure in which the research proposes to use volunteers. The overall responsibility of the Board is to assure that the rights and welfare of subjects are protected. Reference OTSG Regulation 15-2, entitled Boards, Commissions and Committees: HUMAN SUBJECTS RESEARCH REVIEW BOARD.

l. As the administrative office for the HSRRB, the HURRAO is responsible for preparing the minutes of Board meetings in which proposals and protocols are reviewed. The minutes, at a minimum, show members present, provide a record of discussion, document recommendations of the Board concerning proposals and protocols presented, and the record of vote and approval on proposals and protocols. After which, the minutes are presented to the Chairman of the HSRRB for review and recommendation of approval and are later submitted from the HURRAO to TSG for review and approval. TSG is the final approving authority for those proposals and protocols presented before the HSRRB. The HURRAO review process, as specified in paragraph 4, is applicable to TSG approved proposals.

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APPENDIX G

(SEE - HHS FORM 596)

APPENDIX H

RESEARCH ACTIVITIES WHICH MAY BE REVIEWED
THROUGH EXPEDITED REVIEW PROCEDURES

Research activities involving no more than minimal risk and in which the only involvement of human subjects will be in one or more of the following categories (carried out through standard methods) may be reviewed by the Human Use Committee/ Institutional Review Board through the expedited review procedure authorized in 45 CFR 46.110.

1. Collection of hair and nail clippings in a non-disfiguring manner; of deciduous teeth; and permanent teeth if patient care indicates a need for extraction.

2. Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane before or during labor.

3. Recording of data from subjects who are 18 years of age or older using noninvasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (for example, x-rays or microwaves).

4. Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an eight-week period and no more often that two times per week, from subjects 18 years or older and who are in good health and not pregnant.

5. Collection of both supra- and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

6. Voice recordings made for research purposes such as investigations of speech defects.

7. Moderate exercise by healthy volunteers.

8. The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

9. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate subjects' behavior and the research will not involve stress to subjects.

Within USAMRDC, studies concerning the following areas, even if determined to be minimal risk, must be submitted to The Surgeon General (TSG) for approval:

1. Schedule I controlled substances.

2. Radioisotopes.

3. Drug and alcohol abuse.

4. All protocols involving chemical, biological, or nuclear threat agents, and human subjects, regardless of whether the subject is the direct or indirect object of the research, will be submitted to TSG for review. TSG will forward the protocol with his recommendations through appropriate channels to the Under Secretary of Defense for Acquisition.

APPENDIX I

EXEMPT RESEARCH CATEGORIES

(Extracted in part from Title 45, Code of Federal Regulations, Part 46.101 - Protection of Human Subjects)

Research activities in a health-related field in which the only involvement of human subjects will be in one or more of the following categories are exempt from 45 CFR 46 unless the research is covered by other subparts of Part 46:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (a) research on regular and special education instructional strategies, or (b) research on the effectiveness of, or the comparison among, instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), if information taken from these sources is recorded in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

3. Research involving survey or interview procedures, except where all of the following conditions exist: (a) Responses are recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects; (b) the subject's responses, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing or employability, and (c) the research deals with sensitive aspects of the subject's own behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol. All research involving survey or interview procedures is exempt, without exception, when the respondents are elected or appointed public officials or candidates for public office.

4. Research involving the observation (including observation by participants) of public behavior, except where all of the following conditions exist: (a) Observations are recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects, (b) the observations recorded about the individual, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's

financial standing or employability, and (c) the research deals with sensitive aspects of the subject's own behavior such as illegal conduct, drug use, sexual behavior, or use of alcohol.

5. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

6. Flight training, jump training, marksmanship training, ranger training, fire drills, gas drills, handling of explosives.

7. Normal training or other military duties as part of an experiment wherein disclosure of experimental conditions to participating personnel would reveal the artificial nature of such conditions and defeat the purpose of the investigation.

APPENDIX J

GUIDELINE FOR SUBMISSION OF INVESTIGATIONAL NEW DRUG (IND)
ANNUAL REPORTS (21 CFR 312.33)

A sponsor shall within 60 days of the anniversary date that the IND went into effect, submit a brief report of the progress of the investigation that includes:

(a) Individual study information. A brief summary of the status of each study in progress and each study completed during the previous year. The summary is required to include the following information for each study:

(1) The title of the study (with any appropriate study identifiers such as protocol number), its purpose, a brief statement identifying the patient population, and a statement as to whether the study is completed.

(2) The total number of subjects initially planned for inclusion in the study, the number entered into the study to date, the number whose participation in the study was completed as planned, and the number who dropped out of the study for any reason.

(b) Summary information. Information obtained during the previous year's clinical and nonclinical investigations, including:

(1) A narrative or tabular summary showing the most frequent and most serious adverse experiences by body system.

(2) A summary of all IND safety reports submitted during the past year.

(3) A list of subjects who died during participation in the investigation, with the cause of death for each subject.

(4) A list of subjects who dropped out during the course of the investigation in association with any adverse experience, whether or not thought to be drug related.

(5) A brief description of what, if anything, was obtained that is pertinent to an understanding of the drug's actions, including, for example, information about dose response, information from controlled trials, and information about bioavailability.

(6) A list of the preclinical studies (including animal studies) completed or in progress during the past year and a summary of the major preclinical findings.

(7) A summary of any significant manufacturing or microbiological changes made during the past year.

(c) A description of the general investigational plan for the coming year to replace that submitted 1 year earlier. The general investigational plan shall contain the information required under Section 312.23(a)(3)(iv).

(d) If the investigator brochure has been revised, a description of the revision and a copy of the new brochure.

(e) A description of any significant Phase 1 protocol modifications made during the previous year and not previously reported to the IND in a protocol amendment.

(f) A brief summary of significant foreign marketing developments with the drug during the past year, such as approval of marketing in any country or withdrawal or suspension from marketing in any country.

(g) If desired by the sponsor, a log of any outstanding business with respect to the IND for which the sponsor requests or expects a reply, comment, or meeting.

APPENDIX K

CONTRACTOR USE OF HUMAN SUBJECTS, INVESTIGATIONAL DRUGS AND INVESTIGATIONAL MEDICAL DEVICES

1. Definitions:

a. Subject at risk means any individual who may be exposed to the possibility of injury, including physical, psychological, or social, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

b. Investigational drugs. A drug may be considered investigational when the composition is such that --

(1) Its proposed use is not recognized for the use under the conditions prescribed; or its proposed use is not recommended or suggested in its approved labeling. Experts qualified by scientific training and experience evaluate the safety and effectiveness of drugs to make this determination.

(2) Its use has become recognized as investigational, as a result of studies to determine its safety and effectiveness for use under such conditions (21 CFR 312).

c. Investigational medical devices.

(1) A device that is not generally used in the diagnosis, cure, mitigation, treatment or prevention of disease in humans, and recognized as safe and effective.

(2) Research is usually, but not necessarily, initiated to determine if the device is safe or effective (21 CFR 812).

2. Requirements for the Use of Humans:

a. The U.S. Army Medical Research and Development Command (USAMRDC) policies and procedures governing the use of human subjects parallel those of the Department of Health and Human Services (DHHS) as contained in the Code of Federal Regulations, Title 45, Part 46 (45 CFR 46). Assurance of compliance with USAMRDC policy may be documented by submission of a completed Form HHS 596 (Protection of Human Subjects Assurance/ Certification/Declaration). If such documentation is not available, a statement from an approved institutional official

indicating full compliance with 45 CFR 46 may be used, after review by the USAMRDC, to negotiate a special assurance regarding the use of human subjects in the research project.

b. Informed consent statements for the proposed research shall include those details described in 45 CFR 46 and, in addition, the special Department of Defense (DOD) provisions listed in paragraph 3 below. A sample consent form and the advertisement used to recruit subjects, if applicable, should be provided with the proposal. The elements of informed consent are found in paragraph 7 of this regulation (USAMRDC Reg 70-25). Paragraph 4 of this appendix contains guidance for constructing the advertisement notice.

3. Special Human Use Provisions in DOD Funded Research

a. Title 10, U.S.C., Section 980, Requirement for Obtaining Informed Consent states that funds appropriated to the DOD may not be used for research involving a human being as an experimental subject unless:

(1) the informed consent of the subject is obtained in advance; or

(2) in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance.

b. It is DOD policy that the contractor shall make provision for all necessary medical care of research subjects for injury or disease which is the proximate result of participation in the research.

c. DOD Directive 6465.2, dated 19 April 1984, stipulates that organs, tissues, or tissue fluids obtained from an autopsy shall not be used for research or investigational purposes without the expressed written consent of the next of kin. It should be noted that a general autopsy consent may not, in itself, be sufficient. If autopsy tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

d. It is the policy of the USAMRDC that organs, tissues, or tissue fluids obtained from a surgical procedure shall not be used for research or investigational purposes without the expressed written consent of the patient or the patient's legal representative. It should be noted that a consent to perform

surgery may not, in itself, be sufficient. If excised tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

e. It is the policy of the USAMRDC that any anatomical substance (organs, tissues, or tissue fluids) linked by identifiers to a particular person and used for research under a USAMRDC sponsored contract shall be donated for the purpose of research or investigation. The donor shall be the person from whom the substance is removed or, in the event of death or legal disability of the person from whom the substance is removed, the next of kin or legal representative of such person. Donation shall be made by written consent and the donor shall relinquish all ownership and/or rights to the substance. All human anatomical substances used in research under contract shall be lawfully acquired. It should be noted that a general autopsy consent form or a consent to perform surgery, in and of themselves, may not be adequate. If excised or autopsy tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

f. Prisoners of war shall not be used as research subjects.

g. The USAMRDC may inspect contractor records concerning the use of humans as research subjects.

h. The Human Use Review and Regulatory Affairs Office, USAMRDC is the office to which principal investigators are to report any research related illnesses or injuries which have occurred as a result of a subject's participation in an investigational drug/device study sponsored by the Office of The Surgeon General.

4. In accordance with 21 CFR 56.111(a)(3), IRBs are responsible for reviewing the methods used by investigators to recruit subjects. One method of recruiting subjects is through advertisements which should be seen as an extension of the informed consent (21 CFR 50.20, 21 CFR 50.25). IRB review of advertisements is necessary to ensure that the information is not misleading to subjects. The FDA has established guidelines on advertisement for research subjects. Generally, the FDA believes that any advertisement to recruit subjects should be limited to:

a. The name and address of the principal investigator.

b. The purpose of the research and, in summary form, the eligibility criteria that will be used to admit subjects into the study.

c. A straightforward and truthful description of the benefits (e.g., payments or free treatment) to the subject from participation in the study.

d. The location of the research and the person to contact for further information.

The advertisement to be used by the investigator to recruit research subjects must be included with the protocol/proposal submission.

APPENDIX L

VOLUNTEER REGISTRY DATA BASE

1. The intent of the data base is two fold: first, to readily answer questions concerning an individual's participation in research conducted or sponsored by the Command; and second, to ensure that the Command can exercise its "duty to warn." The "duty to warn" is an obligation incurred by Commanders to ensure that research volunteers are adequately informed concerning the risks involved with their participation in research, and to provide them with any newly acquired information that may affect their well-being when that information becomes available. The duty to warn exists even after the individual volunteer has completed his or her participation in research. To accomplish this, a system must be established which will permit the identification of volunteers who have participated in research conducted or sponsored by USAMRDC and action must be taken to notify volunteers of newly acquired information.

2. The data base must contain items of personal information, for example, name, Social Security number, etc., which subjects it to the provision of The Privacy Act of 1974. Within USAMRDC this data base consists of the data bases maintained at the individual laboratory or other research site and the archival data base maintained at USAMRDC Headquarters.

3. For each human subject enrolled in a research protocol conducted at a USAMRDC laboratory a Volunteer Registry Data Sheet (USAMRDC Form 60-R) is to be completed. The information is then to be entered into the laboratory data base. The information from the laboratory data base is exported to the Headquarters archival data base upon completion of a research protocol or annually, whichever occurs first. The information is stored in the Headquarters data base for a minimum of 75 years.

APPENDIX L (Continued)

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PAGE L-3 & L-4 SEE - USAMRDC FORM 60-R

The proponent agency of this regulation is the Human Use Review and Regulatory Affairs Office. Users are invited to send comments and suggested improvements on DA Form 2028 (Recommended Changes to Publications and Blank Forms) direct to Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD-HR, Fort Detrick, Frederick, Maryland 21701-5012.

FOR THE COMMANDER:

OFFICIAL:

LEON L. HOLLAND
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